#### Azad K. Kaushik 9, Currie Drive, Morriston, Ontario NOB 2C0 Canada

e-mail: <u>kaushik.azad@gmail.com;</u> akaushik@uoguelph.ca Phone: +1 (519) 760 2297 Dr. Azad K. Kaushik, is an internationally recognized Immunologist at the University of Guelph since 1991 with expertise in Immunology, Biotechnology and Veterinary Medicine. Dr. Kaushik has education and professional experience spread over India, France, USA, Switzerland and Canada. Dr. Kaushik's research contributions are recognized internationally for advancing knowledge in antibody genetics in health and disease. He has published over 100 research articles and book chapters, and published two books: Molecular Immunobiology of Self-Reactivity' (1992), a major advance in understanding of the systemic autoimmune diseases in the context of immune function; and Comparative Immunoglobulin Genetics' (2014) that highlights his discoveries on cattle antibodies and their application for development of new anti-viral and anticancer antibody based drugs. His research has opened new opportunities for developing novel types of drugs and vaccines for disease prevention in humans and other species. He has trained significant number of MSc, PhD and post-doctoral scientists. These students have won 11 awards and are working at leading institutions in academia, government and industry. He holds four US and Canadian patents related to his discoveries on cow antibodies. He is on the editorial board of several immunology journals and is a Consultant to various international organizations like US Veterinary Immune Reagent Network and Comparative Immunoglobulin Workshop in USA and IMGT (International ImMunoGeneTics Information System), France. He was recognized as The Esther Z. Greenberg Honors Chair in Biomedical Research and Visiting Professor, Oklahoma Medical Research Foundation, USA, in 1998. He received BVSc&AH (Honors) in 1976 and MVSc (1978) from the Faculty of Veterinary Science, Hisar, Haryana, India followed by 'Docteur es Science' with a mention 'Tres Honorable', (1987) from Pasteur Institute (Univ. of Paris VII), Paris, France. He engaged in advanced studies at leading institutions like Cold Spring Harbor Laboratory, Albert Einstein College of Medicine in New York and Lawrence National Laboratory, Berkley.

#### I. Stellar achievement

• Scientific discovery of the cow antibodies that are largest known to exist in a species that open doors of opportunity to develop novel drugs (against cancer, viruses and autoimmune disease), immunomodulators and vaccines.

- 1. Saini, S. S., Allore, B., Jacobs, R. M. and Kaushik, A. 1999. Generation of an exceptionally long CDR3H, with multiple cysteine residues, provides a novel mechanism of antibody diversity. European Journal of Immunology. 29:2420-26.
- 2. Ramsland, P. A., Kaushik, A., Marchalonis, J. J. and Edmunson, A. B. 2001. Incorporation of long CDR3 into V domains: Implications for the structural evolution of the antibody-combining site. Exp. Clin. Immunogenetics. 18:176-98.
- 3. Saini, S.S. and Kaushik, A. 2002. Extensive CDR3H length heterogeneity exists in bovine fetal VDJ rearrangements. Scandinavian Journal of Immunology. 55:140-48.
- 4. Kaushik, A., Shojaei, F. and Saini, S. S. 2002. Novel insight into antibody diversification from cattle. Veterinary Immunology & Immunopatholgy 87:347-350.
- 5. Saini, S. S., Kaushik, A., Basrur, P. and Yamashiro, S. 2003. Ultrastructural and immunological characteristics of xenogeneic hybridomas originating from bovine leukemia virus infected cattle. Veterinary Pathology. 40:460-64.
- Shojaei, F., Saini S. S., Kaushik A. K. 2003. Unusually long germline D<sub>H</sub> genes contribute to the generation of exceptionally long CDR3H in bovine antibodies. Molecular Immunology 40:61-67.

- 7. Saini, S.S., Farrugia W., Muthusamy N., Ramsland, P. A. & Kaushik, A.K. 2007. Structural evidence for a new IgG1 antibody sequence allele of cattle. Scandinavian Journal of Immunology. 65:32-38 (Journal Cover Picture Citation).
- 8. Koti, M., Kataeva, G. and Kaushik, A. K. 2008. Organization of DH-gene locus is distinct in cattle. Dev. Biol. (Basel) 132:307-13.
- 9. Kaushik, A. K., Kehrlis Jr., M. E., Ng, S., Kurtz, A., Koti, M., Shojaei, F. Saini, S. 2009. Somatic mutations and isotype restricted exceptionally long CDR3H contribute to antibody diversification in cattle. Vet. Immunol. Immunopathol. 127:106-13.
- Koti, M. and Kaushik, A. K. 2010. Novel Atypical Nucleotide Insertions specifically at VH-DH Junction Generate Exceptionally Long CDR3H in Cattle Antibodies. Molecular Immunology. 47: 2119-28.
- 11. Koti, M., Nagy, E. and Kaushik, A. K. 2011. A single point mutation in framework region 3 of heavy chain affects viral neutralization dynamics of single-chain Fv against bovine herpes virus type-1. Vaccine. 29: 7905-12 (DOI: 10.1016/j.vaccine.2011.08.077).
- 12. Pasman, Y., Nagy, E., and Kaushik, A. K. 2012. Enhanced bovine herpes virus type-1 neutralization by multimerized scFvs regardless of differential glycosylation. Clinical and Vaccine Immunology. 19(8): 1150-57 (DOI: 10.1128/CVI.00130-12).
- Pasman, Y., Bhogal, R. and Kaushik, A. K. 2013. Novel Perspective on Antibody Diversification from Bovine Immunoglobulin Genetics. Chapter 1, In: Cattle: Domestication, Diseases and Environment. (George Liu Editor), p.1-23. Nova Science Publisher Inc., New York 11788-3619, USA.
- 14. Koti, M., Saini, S.S., Sachan, A. and Kaushik, A. K. 2014. Engineered Bovine Antibodies in Development of New Therapeutics, Immunomodulators and Vaccines. Antibodies 3: 205-214.
- 15. Pasman, Y. and Kaushik, A. K. 2014. Bovine immunoglobulin genetics a phylogenetic perspective. In: Comparative Immunoglobulin Genetics (A. K. Kaushik, and Y. Pasman, Editors). Apple Academic Press, Toronto, Canada. p.,187-221.
- Aida, Y., Takeshima, S.-N., Baldwin, C. L. and Kaushik, A. K. 2015. Bovine Immunogenetics. In: The Genetics of Cattle (Dorrian J. Garrick, and Anatoly Ruvinsky, Editors). 2<sup>nd</sup> Edn. CAB International. p.,153-191.
- 17. Pasman, Y. and Kaushik, A. K. 2016. VH and VL domains of polyspecific IgM and monospecific IgG antibodies contribute differentially to antigen recognition and virus neutralization functions. Scandinavian Journal of Immunology. 84: 28-38.
- Pasman, Y. and Kaushik, A. K. 2016. Exceptionally long CDR3H of bovine scFv antigenized with BoHV-1 B-epitope generates specific immune response against the targeted epitope. Molecular Immunology. 77, 113-125.
- 19. Pasman, Y., Daniele Merico and Kaushik, A. K. 2017. Preferential expression of IGHV and IGHD encoding antibodies with exceptionally long CDR3H and a rapid global shift in transcriptome characterizes development of bovine neonatal immunity. Developmental and Comparative Immunology. 67, 495-507.
- Damani-Yokota P, Gillespie A, Pasman Y, Merico D, Connelley TK, Kaushik A, Baldwin C. L. 2018. Bovine T cell receptors and γδ WC1 co-receptor transcriptome analysis during the first month of life. Dev Comp Immunol. 88:190-199. (doi: 10.1016/j.dci.2018.07.023)
- 21. Kaushik, A.K., Kandavel, H., Nalpathamkalam, T., Pasman, Y., 2021. Bovine neonate is deficient in innate immunity at birth. Mol Immunol 133, 101-109.
- 22. Kaushik, A.K., Kandavel, H., Nalpathamkalam, T., Pasman, Y., 2022. Developing B-lymphocytes

in bovine neonates are deficient in central tolerance at birth. Mol Immunol. Submitted

#### • Discovery of Cow Mega-bodies for Next Generation Therapeutics

• Research Highlight and Interview, 'Mega-antibodies: next-generation therapeutics' in in the journal 'International Innovation', 2014,161:94-95 (www.internationalinnovation.com); Youtube: https://youtu.be/m6VBJJF2BjU (CTV Kitchener news).

#### • Development of antibody based anti-viral drugs against bovine respiratory disease in cattle

- 1. Koti, M., Farrugia, W., Nagy, E., Ramsland, P.A., Kaushik, A.K. 2010. Construction of singlechain Fv with two possible CDR3H conformations but similar inter-molecular forces that neutralize bovine herpes virus I. Mol. Immunol. 47: 953-960.
- 2. Koti, M., Nagy, E. and Kaushik, A. K. 2011. A single point mutation in framework region 3 of heavy chain affects viral neutralization dynamics of single-chain Fv against bovine herpes virus type 1. Vaccine. 29: 7905-12.
- 3. Pasman, Y., Nagy, E., and Kaushik, A. K. 2012. Enhanced bovine herpes virus type-1 neutralization by multimerized scFvs regardless of differential glycosylation. Clinical and Vaccine Immunology. 19(8): 1150-57.

#### • Books:

- 1. Bona, C. and Kaushik, A. (editors) 1992. Molecular Immunobiology of Self- Reactivity. Marcel Dekker Inc., New York, USA.
- 2. Kaushik, A. K. and Pasman, Y. (editors) 2014. Comparative Immunoglobulin Genetics. Apple Academic Press, Oakville, Ontario, Canada.

# • Patents: Immunotechnology related to disease resistance, vaccine development and antibody engineering

- 1. "Novel bovine VDJ cassette, BF1H1, suitable for antigenization", U.S. Patent, No. 6,740,747, Granted 2004.
- 2. "Bovine D-genes and their application", US patent No. 7,196,185, Granted 2007
- 3. Development of neutralizing ScFvs against Bovine Herpes Virus type-1 for prevention, therapy and diagnosis of Infectious Bovine Rhino-tracheitis (PCT International Patent Application filed July, 2008;)
  - a. US Patent No. 8,383,115 B2 Granted February 26, 2013
  - b. Canadian Patent No. CA 2693137, Granted October 29, 2013

#### • Research Citations in textbooks

- 1. Veterinary Immunology: An Introduction, 7<sup>th</sup> ed. (2004) I. Tizard, W.B. Saunders Co., Chapter 14, p.164.
- 2. Clinical Immunology of the Dog & Cat, 1<sup>st</sup> ed. (1999) Michael J. Day, ISU Press, Iowa, Chapter 15, p. 284.

3. The Genetics of Cattle, 1<sup>st</sup> ed. (1999) - Ruedi Fries and Anatoly Ruvinsky, CABI (www.cabi.org), Chapter 7 •Hundreds of unique DNA Sequences deposited and annotated via GenBank in advancement of science and knowledge

#### • Invited lectures

Over 100 invited lectures in USA, Canada, Europe, Latin America and Asia

#### • Education and Training

- 1. Trained 5 MSc, 3 PhD and 6 post-doctoral scientists.
- 2. Trained Thousands of DVM and BSc Honors level students

#### II. Entrepreneurial achievements

• Founded ImmVacca start up for immunology Consultancy, commercialization of new technology on cow antibody based drugs and vaccines.

#### III. Professional achievements and international involvement

- Indo-French Research Scholar (1983-86)
- Medical Scholar, French Medical Research Foundation, Paris, France (1986-87)
- Lupus Fellow, The SLE Foundation, New York, USA (1988)
- Consultant, US Veterinary Immune Reagent Network, 2006-present
- (www.umass.edu/vetimm/ruminants/index.html).
- Faculty, International Union of Immunological Societies (2002-08)
- IMGT Expert (Bovine Immunoglobulin) 2010-; (http://imgt.cines.fr/textes/IMGTindex/IMGTexperts.html)
- "Plaque of Honor" for 'Discovery of Novel Cow Antibodies', National Academy of Agricultural Sciences, New Delhi, India, 2015 (naasindia.org/documents/Public%20Lecture.doc).
- Research Highlight and Interview, 'Mega-antibodies: next-generation therapeutics' in the journal 'International Innovation', 2014,161:94-95 (www.internationalinnovation.com).
- Member, Editorial Board, Journal of Clinical Immunology & Immunopathology Research, Journal of vaccine and Immunization
- Member, American Association of Immunologists, Canadian Society of Immunology, Academy of Veterinary Allergy & Clinical Immunology.
- Co-Chair, Session on "The Immune Repertoire", American Association of Immunologists Meeting/Experimental Biology, 1998, San Francisco, April 18-22, 1998.
- Chair, Session on "Ig and TcR Genes", 5<sup>th</sup> International Veterinary Immunology Symposium, Ludhiana, India, November 1998.
- Co-Chair, 'Lymphocyte Development' Workshop, Canadian Society for Immunology Meeting, Chateau Lake Louise, April 2001.
- Co-Chair, Session on "Comparative Immunoglobulin Structure and Function", American Association of Immunologists Meeting/Experimental Biology, 2008, San Diego, April 5-9, 2008.

- Chair, Ontario Graduate Studies Scholarship Award Committee Panel (2002), Canada.
- Member, NIH Grant Review Panel on 'Specialized Centers of Research on Systemic Lupus Erythematosus' (2002), USA.
- Member, American Association of Immunologists, Canadian Society of Immunology, Canadian Society of Microbiology, New York Academy of Science, Academy of Veterinary Allergy & Clinical Immunology.
- Ad hoc Reviewer, Journal of Immunology, Autoimmunity, Viral Immunology, Molecular Immunology, Developmental and Comparative Immunology, Veterinary Immunology and Immunopathology, Veterinary Microbiology, Canadian journal of Microbiology
- Ad hoc Reviewer, Grant-in-Aid, Canadian Arthritis Society Grant-in-Aid, Medical Research Council, NSERC Canada, NIH SCOR Program, Health Canada, Michael Smith Foundation for Health Research, Canadian Foundation for Innovation
- Editor-at-Large, Marcel Dekker Inc., New York; Member, Editorial Board, Journal of Veterinary Allergy & Clinical Immunology
- Curator, "Bovine VH and Vλ Genes", Comparative Immunoglobulin Workshop, USA. (http://www.medicine.uiowa.edu/cigw/cow.htm), 2001-10; Reappointed 2010 – present.
- Plaque of Honor for Discovery of Novel Cow Antibodies', National Academy of Agricultural Sciences, New Delhi, India, 2015 (naasindia.org/documents/Public%20Lecture.doc).
- Member, American Association of Immunologists Veterinary Immunology Committee, 2015 2018.
- Co-Chair, Session on Vaccines 2, International Congress of Immunology 2016, Melbourne, Australia.

# IV. Contribution to the community Founder President, World Brahman Federation Canada that promotes Dharma and values in the

- Founding President, National Alliance of Indo-Canadians; Chair, Organizing Committee for Community Reception for Indian Prime Minister Narendra Modi, on bilateral visit, attended by Canadian Prime Minister Stephen Harper, that enhanced Canada-India relations.
- Founder President, World Brahman Federation Canada that promotes Dharma and values in the society (www.wbfcanada.org)
- Public speaker and influencer in the community on matters concerning human consciousness, Dharma and civilization. Value based education to youth to become lawabiding citizens who are an asset to the society and contribute towards advancing aspirations as Canadians.
- "Bharat Gaurav Award" (Honor of India) in 2018 at the House of Commons, UK.
- "Certificate of Appreciation" (2019), for volunteerism and outstanding contributions that helped enhance quality of life for Canadians.
- International Award, 'Brahmdeep' for community service by Global Brahman Confederation, Los Angeles, USA, 2012.
- Organized two expeditions to Himalayas and climbed Mount Ladhaki (18,600' ft) and Mount Thailoo (20,000' ft).

# Cow antibodies



Veterinarian and researcher **Dr Azad Kumar Kaushik** is studying antibodies from cattle in the hope of developing novel drugs and vaccines. Here, he reveals his fortuitous entry into the field, and the talented team members who have made his work possible

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### What intrigues you about the mechanisms of immunity?

As a veterinary medicine student, I was intrigued by the generation of immunity against a variety of infectious agents, especially the concept of an almost endless generation of diversity, while being tolerant to self-constituents. This led me to the Pasteur Institute to study the origin of autoantibodies against red blood cells involved in haemolytic anaemia, seen in systemic autoimmune disease.

### Can you discuss some of your key findings?

We noted that the same host genetic elements encoded physiological autoantibodies, antibodies to infectious agents and pathogenic autoantibodies, using similar mechanisms. Our later research showed that impaired B-lymphocyte development, due to underlying genetic factors evident at birth, provides the trigger that gets amplified by environmental factors resulting in production of pathogenic autoantibodies seen in systemic autoimmune disease like lupus. These studies of the immune system in health and disease across species led me to bovine antibodies upon my return to veterinary profession.

### Why do you focus specifically on the bovine immune system?

Given their medical significance, most studies had focused on human and mouse immune systems. As a veterinarian, I was aware that the immune system must have evolved for each species to meet varying individual host defence requirements. When taking up the position of Clinical Immunologist at the Ontario Veterinary College – a move away from the human medicine environment – I needed to embark upon a new research path. I decided to study the bovine immune system as I knew that little was understood about cattle antibody genetics.

### Could you explain the need for new antibody-based vaccines?

There are many controversies surrounding vaccines in the public domain. Some of the concerns may be related to the quality of available vaccines or components; alternatively, individual host genetics might influence response to a particular vaccine. Hence, there is a need for better quality vaccines against various infectious agents that have minimal side effects and are suitable for use in large populations, including immunocompromised individuals and neonates. Furthermore, successful vaccines are yet to be developed against certain pathogens, such as HIV and *Plasmodium falciparum*.

#### With a world-leading team in bovine antibody genetics, what distinguishes your laboratory from others?

My laboratory is small with limited resources, but rich in human intellect and ingenuity; a nurturing environment exists for advancing scholarships, exchanging ideas and flourishing creativity. I have had the good fortune of working with some outstanding colleagues, whose passion, creativity and efforts put us in the top league of bovine immunoglobulin genetics. The commonwealth scholar, Dr Surinder S Saini, discovered the exceptionally long CDR3H in cattle antibodies, at a time when cDNA sequencing was a time-consuming challenge. Dr Farbod Shojaei discovered the single long germline IGHD gene in the cattle, capable of encoding 49 codons of CDR3H. Dr Madhuri Koti discovered the molecular basis of exceptionally long CDR3H in cattle antibodies beyond germline potential via CSNS insertion. While Dr Koti first engineered bovine scFv that neutralises BoHV-1. Ms Yfke Pasman. enhanced bovine scFv's anti-viral potency via multimerisation. Ms Pasman is currently enhancing the understanding of cattle antibody structure-function relationships for developing the next generation of vaccines, immunodiagnostics and antiviral drugs. Such wonderful, dedicated and passionate colleagues distinguish our laboratory from others in the field.

## Mega antibodies: next-generation **therapeutics**

Researchers from a worldleading laboratory at the **University of Guleph** in Canada are studying the antibodies of cows, paving the way for new vaccines and medicines to prevent and treat human disease

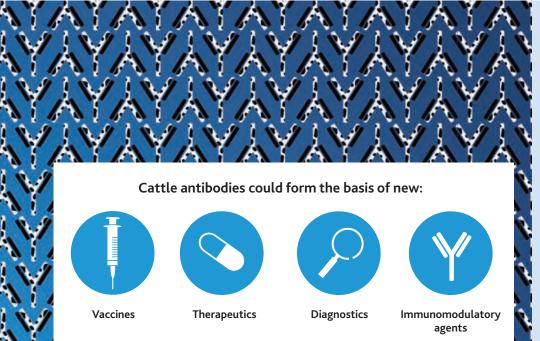
WHEN ASKED TO think about cows and the resources they provide, milk and beef might be the first to come to mind, but there is actually something else produced by cows – unique to them – that makes them a valuable therapeutic resource: antibodies. Cows produce the largest sized antibodies of the whole of the animal kingdom. These massive antibodies are distinctively poised for more effective at attacking diverse bacteria and viruses, and have the potential for use in humans as well.

Dr Azad Kumar Kaushik, Associate Professor of Immunology at the University of Guleph in Ontario, was captivated by the processes of immunity at an early age and has been working on them, in humans and animals, ever since. After years of studying the structure of immune systems across multiple species, his laboratory is now focused on the bovine immune system.

Supported by the Canadian Natural Science and Engineering Research Council (NSERC), Kaushik's investigations have identified and classified the genetic elements encoding bovine antibodies, as well as discovered novel mechanisms that enable production of such a vast array of antibodies beyond germline potential. His current research is conducted with a view to engineering antibodies for next-generation therapeutic and diagnostic tools.

#### **OVERCOMING LIMITED DIVERSITY**

Kaushik's investigations of the bovine immune system began by identifying the genetic elements that encode the antibody. The team discovered that the limited germline diversity of the cow genome has led to the creation of the largest antibodies known in any species. Exceptionally long third complementary determining regions of



the heavy chain (CD3RH) are generated, over 50 amino acids in length. As well as creating atypical antigen-binding site diversity, the size of the antibodies also makes them suitable to work with. A major barrier to successful antibody-based immunotherapies in the past has been the lack of a suitable vehicle to transfer immunity from animals to the lab, but the size and flexibility of the bovine antibody overcomes this. In the longer term, modified bovine antibodies could be used to target diseases where traditional therapies fail, helping the body to recognise and protect from pathogens that would otherwise go undetected.

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The researchers went on to find that CD3RH is encoded by a single, again unusually long, gene – IGHD – which is capable of encoding a striking 49 codons. It does so in concert with the insertion of a conserved short nucleotide sequence (CSNS) at a specific junction of *IGHV* and *IGHD* that further increases CDR3H size. Building on these past successes, Kaushik's team is presently focused on the next stage on from genetics: structure and function.

Antibodies are multi-functional molecules, they recognise antigens, engulf pathogens, and much more. Each function is designated to a specific structure. "It is therefore possible to genetically manipulate and generate an engineered molecule for a desired function," Kaushik explains.

#### TACKLING A BOVINE VIRUS

Through his studies, Kaushik successfully developed powerful antibody fragments called single chain fragment variables (scFv). Importantly, these scFv are able to neutralise Bovine Herpes Virus-1 (BoHV-1), a major problem in North America that costs the cattle industry up to \$100 million each year in Canada alone. The team took genetic material from a cell producing antibodies against BoHV-1 and modified the gene producing the antibody. They inserted the new gene into yeast cells to produce the antibodies en masse, before adding them to infected cells to investigate their ability to attack the virus. Kaushik's scFv was found to neutralise the virus, preventing its attachment to host cells and subsequent replication.

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Kaushik hopes to develop drugs and vaccines for humans, particularly against common infections of the intestine

#### **MAKING MEGABODIES**

Based on these promising findings, Kaushik hopes to develop drugs and vaccines for humans, particularly against common infections of the intestine. The potential here is huge. By coupling the antibodies with drugs, they could be used to target specific locations in the body to destroy the pathogen or diseased tissue. "Our discovery of large sized bovine antibodies, which I call 'megabodies', will have a huge impact not just on veterinary science but also on human medicine," Kaushik enthuses. In the future, he hopes to capitalise on the rise in popularity of using antibodies for therapeutic purposes by further developing his research on structure-function to understand, exploit and even engineer multifunctional antibodies to prevent and treat disease, setting his sights on complex autoimmune diseases and even cancer.

#### INTELLIGENCE

#### POST GENOMIC STRUCTURAL AND FUNCTIONAL ASPECTS OF ANTIBODY IN HEATH AND DISEASE

#### OBJECTIVE

To advance knowledge of the development, 'structure-function' relationships and regulation of humoral immunity in health and disease aimed at designing antibodybased therapeutics, diagnostics and novel vaccines across species, including humans.

#### **KEY COLLABORATORS**

Dr Éva Nagy, University of Guelph, Canada

Dr Paul A Ramsland, Burnet Institute, Australia

#### FUNDING

Natural Sciences and Engineering Research Council of Canada (NSERC)

#### CONTACT

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www.nserc-crsng.gc.ca/ase-oro/Details-Detailles\_eng.asp?id=475525

DR AZAD KUMAR KAUSHIK has published over 85 research articles, two books and four patents on cattle antibodies. He is Consultant to several international organisations (USVIRN and ClgW in USA, and IMGT in France). He was recognised as The Esther Z Greenberg Honors Chair in Biomedical Research, Oklahoma Medical Research Foundation, USA, in 1998. He received BVSc&AH (Honors) in 1976 and MVSc (1978) from the Faculty of Veterinary Science, Hisar, India; followed by a Docteur es Science (DSc) in1987 from the Pasteur Institute (University of Paris VII), Paris, France.



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Current position:	Adjunct Professor of Immunology, University of Guelph, Guelph, Ontario N1G 2W1
Personal data:	Overseas Citizen of India, Canadian Citizen; Proficient in English, French, Hindi

#### **Education:**

- **1987** D.Sc. (*Docteur es Science*), Pasteur Institute (Univ. of Paris VII), Paris, France Mention: "Tres Honorable"
- **1978 M.V.Sc.** (Veterinary Microbiology & Immunology), Faculty of Veterinary Medicine (Haryana Ag. University), Hisar, India
- **1976 B.V.Sc./DVM**, Faculty of Veterinary Medicine (Haryana Ag. University), Hisar, India Graduated with **'Honours'**

[Academic License (No. 4795), College of Veterinarians of Ontario]

#### **Research Interests**

Molecular Immunoglobulin Genetics, Antibody Engineering and Transgenesis, Autoimmunity and Systemic Autoimmune Disease, Therapeutics and Vaccines, Immunodiagnostics, Clinical Veterinary Immunology

#### **Advanced Studies**

- Phage Display Technology', Cold Spring Harbor Laboratory, New York, USA (1997)
- Bioinformatics, Lawrence National Laboratory, Berkley, USA (2004)
- Gene transfer Technology' (Mouse Developmental genetics), Albert Einstein College of Medicine, New York, USA (2004)
- Bioinformatic Analysis of Next Generation Sequencing Data', National Institutes of Health, Bethesda, USA (2014)

#### Experience

- 1979-1983 Assistant Professor (Tenured), Department of Vet. Microbiology & Immunology, Faculty of Veterinary Medicine, Haryana Ag. University, Hisar, India.
- 1983-1987 Visiting Scientist, Departments of Immunology and medicine, Pasteur Institute, Paris, France.
- 1987-1990 Research Associate, Department of Microbiology, Mount Sinai School of Medicine, New York, U.S.A.
- 1990-1991 Assistant Research Professor, Dept. Medical Biochemistry, Faculty of Medicine, University of Geneva, Geneva, Switzerland.
- 1991-Present Professor of Immunology, Department of Pathobiology/Microbiology, University of Guelph, Ontario, Canada.
- 01-08/1998 Visiting Professor and Greenberg Scholar, Oklahoma Medical Research Foundation, Oklahoma City, USA.

#### **Honors and Distinctions**

- Indo-French Research Scholar (1983-86)
- Medical Scholar, French Medical Research Foundation, Paris, France (1986-87)
- Lupus Fellow, The SLE Foundation, New York, USA (1988)
- The Esther Z. Greenberg Honors Chair in Biomedical Research and Visiting Professor, Oklahoma Medical Research Foundation, USA (1998)
- Consultant, US Veterinary Immune Reagent Network, 2006-present (http://www.umass.edu/vetimm/ruminants/index.html); (http://www.umass.edu/vetimm/docs/Bovine Poster IVIS.pdf.)
- Faculty, International Union of Immunological Societies (2002-08)
- Contributor and Curator, "Bovine  $V_H$  and  $V\lambda$  Genes", Comparative Immunoglobulin Workshop (<u>http://www.medicine.uiowa.edu/cigw/cow.htm</u>) 2001-present.
- IMGT Expert, 2010 present (http://imgt.cines.fr/textes/IMGTindex/IMGTexperts.html)
- Distinguished Speaker, Antibody Design and Discovery Conference, Jun 07-08, 2012, San Diego, CA, USA
- Editor-in-Chief, Veterinary Microbiology and Immunology Series (http://www.appleacademicpress.com/category.php?id=2)
- Member, Editorial Board:
  - Journal of Biomedical Sciences (1996 present) <u>http://www.jbiomeds.com/editors.php</u>
  - o Journal of Veterinary Allergy and Clinical Immunology (1996-2001)
  - o Journal of Vaccines and Immunization (2011 2014),

(http://www.nobleresearch.org/Journal/EditorialBoard/3)

- Research in Immunology (2013-present)
- Journal of Clinical and Experimental Genetics (2014 present) (<u>http://www.annexpublishers.com/journals/journal-of-clinical-and-experimental-genetics/editorial-board.php</u>)
- International Award, Brahmdeep for community service by Global Brahman Confederation, Los Angeles, USA, 2012.
- Plaque of Honour for Discovery of Novel Cow Antibodies', National Academy of Agricultural Sciences, New Delhi, India, 2015 (naasindia.org/documents/Public%20Lecture.doc).
- Research Highlight and Interview, 'Mega-antibodies: next-generation therapeutics' in in the journal International Innovation', 2014,161:94-95 (www.internationalinnovation.com).
- Member, American Association of Immunologists Veterinary immunology Committee, 2015 -2018.
- Co-Chair, Session on Vaccines 2, International Congress of Immunology 2016, Melbourne, Australia.
- Prestigious "Bharat Gaurav" Award at the House of Commons, London, U. K. Sanskriti Yuva Sanstha

#### **Research Discoveries**

- Development of novel cow antibody based vaccines and drugs
- Discovery of unique antibodies with an exceptionally long CDR3H in cattle antibodies.
- Novel genetic elements encoding antibodies
- Novel mechanisms of antibody diversification
- Origin of autoantibodies in natural autoimmunity and systemic autoimmune disease

#### **Research Applications**

- Development of scFv capable of virus neutralization
- Development of new vaccines via antigenization of scFvs

#### **Research Profile**

I have an internationally recognized established research program focused on fundamental aspects of humoral immunity in health and disease consistently supported by NSERC Discovery, equipment and OMAFRA research grants since 1992. Specifically, my research is focused on understanding autoimmunity and systemic autoimmune disease and dissecting immunoglobulin

genetics aimed at developing next generation of antibody-based immunotherapeutics and vaccines. My research contributions in the field include: 2 Books, 88 Peer-reviewed Research articles and book chapters, 4 patents (plus 1 applied) and 106 invited or research presentations at conferences. Some of my published research is cited in the immunology textbooks.

My early research led to identification of genetic elements encoding autoantibody that for the first time demonstrated that the same genetic elements that defended host against harmful agents encoded pathogenic autoantibodies involved in systemic autoimmune disease, for example, Lupus. This school of thinking that influenced the field of autoimmunity, from 'horror autotoxicus' to physiological autoreactivity, and is outlined in the book Molecular Immunobiology of Self-Reactivity published in 1992 by Marcel Dekker Inc., New York, USA. This led my research to focus on understanding the construction of primary antibody repertoire in health and disease. Apart from identifying new genetic elements, my studies of variable kappa genes in mice broke the prevailing dogma of accessibility-related variable gene expression. I showed enormous plasticity in the construction of primary antibody repertoire because of stochastic heavy and light chain pairing, though exceptions exist. Further, my laboratory demonstrated that a higher expression of kappa light chains in mice resulted, in part, from counter selection of lambda light chains to limit self-reactivity in the primary antibody repertoire. At terminal autoimmune disease state, my laboratory showed that pathogenic IgM autoantibodies had unique structural features in mice, consistent with clonal selection but without somatic mutations. My laboratory further demonstrated that the threshold of B-cell selection during ontogeny influenced the generation of pathogenic IgM autoantibodies involved in the pathogenesis of systemic autoimmune disease. My seminal contributions on the origin of pathogenic IgG and IgM autoantibodies in systemic autoimmune disease have had profound implications on developing therapeutic approaches and disease management strategies targeting B-lymphocytes.

I extended the studies on construction of humoral immune system to cattle that led us to identify and classify the genetic elements encoding bovine antibody. My laboratory has the world lead in bovine immunoglobulin genetics where I am recognized internationally as an expert in the field, for example, IMGT Expert (International Immunogenetics Information System, France; http://www.imgt.org/IMGTindex/ IMGTexperts.php), Curator, Comparative Immunoglobulin Workshop (http://www.healthcare.uiowa.edu/ cigw/animals/cow.htm Univ. of Iowa, USA). My laboratory discovered that some bovine antibodies are the largest known to exist in any species because of an exceptionally long CDR3H, called Megabodies, generated by recombination of unique genetic elements (longest DH gene) involving novel antibody diversification mechanisms. The exceptionally long CDR3H of these antibodies generates a unique antigen-binding site with structural features resulting in atypical conformational diversity. This seminal discovery has gained attention throughout the world and has spurred research for developing new therapeutics using the unique structural features of the antigencombining site generated by large sized CDR3H. These advances in knowledge are outlined in my book, Comparative Immunoglobulin Genetics\_published in 2014 by Apple Academic Press, CRC Press, New Jersey USA. This discovery was highlighted as Mega-antibodies: next-generation therapeutics in the journal 'International Innovation' in 2014. I have now developed for the first-time transcriptome reference signatures of immunocompetence in the bovine newborn, which is relevant to developing neonatal vaccination strategies. I also show that antibodies with exceptionally long CDR3H play an important role in the acquisition of neonatal humoral immunity in cattle.

I extended the knowledge gained from bovine immunoglobulin genetics to its application in developing next generation of antibody-based immunotherapeutics and vaccines. My laboratory developed the first bovine antibody fragment, called scFv (single chain fragment variable), capable of neutralizing bovine herpes virus type-1 (BoHV-1) and enhanced its viral neutralizing potency by multimerizing it. This provides first antibody fragment based anti-viral drug against an important cattle pathogen. My laboratory recently showed 'proof of concept' of developing antibody fragment-based next generation of vaccines by exploiting the exceptionally long CDR3H of bovine antibody.

To conclude, research contributions of my laboratory have led to the following research advances and applications:

- Origin of autoantibodies in natural autoimmunity and systemic autoimmune disease
- Skewed development of primary antibody repertoire in systemic autoimmune disease
- Discovery of unique antibodies with an exceptionally long CDR3H in cattle.
- Identification of new and unique genetic elements encoding bovine antibodies
- Novel mechanisms of antibody diversification
- Development of bovine antibody fragment capable of virus neutralization
- Development of new bovine antibody fragment based vaccines via antigenization

#### Patents:

- "Novel bovine VDJ cassette, BF1H1, suitable for antigenization", U.S. Patent, No. 6,740,747, Granted 2004.
- "Bovine D-genes and their application", US patent No. 7,196,185, Granted 2007.
- "Development of neutralizing ScFvs against Bovine Herpes Virus type-1 for prevention,

therapy and diagnosis of Infectious Bovine Rhino-tracheitis"

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- **4. Kaushik, A.**, Grover, Y. and Pandey, R. Immunity to buffalopox virus. **6th Intl. Congr. Virol.** Sendai, Japan, September 1-7, 1984.
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- 24. Saini, S. S. and Kaushik, A. Bovine variable region immunoglobulin heavy chain genes: Structural analysis and genomic complexity. ASBMB/ASIP/AAI Joint Meeting. New Orleans, June, 1996 (Saini, S. S., and A. Kaushik. 1996. Bovine variable-region immunoglobulin heavy chain genes - Structural analysis and genomic complexity. FASEB J. 10:991, A1171).
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- 30. Saini, S. S., Allore, B., Jacobs, R. M. and Kaushik, A. 1998. Generation of an exceptionally long CDR3H, with multiple cysteine residues, provides a novel mechanism of antibody diversity. FASEB/AAI Joint Meeting. San Francisco, USA, May 1998 (FASEB J. 12:A885-A885, 5124).
- 31. Saini, S.S. and Kaushik, A. Allelic and splice site-associated variants of bovine IgM

antibodies. International Congress of Immunology, New Delhi, India, November 1998.

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- **33.** Saini, S.S. and **Kaushik, A.** Restricted VH+V $\lambda$  pairings occur in bovine IgM antibodies with exceptionally long CDR3H. **FASEB/AAI Joint Meeting**. Washington D.C., March 1999.
- **34.** Cassady, R.L. and **Kaushik, A.** Increased negative B cell selection impairs neonatal IgM repertoire. Canadian Society for Immunology Meeting, Chateau Lake Louise, April 2001.
- **35.** Saini, S.S. and **Kaushik, A**. Structural and functional properties of bovine Vλ-light chains. **Canadian Society of Immunology Meeting**, Chateau Lake Louise, Canada, April 2001.
- 36. F. Shojaei, Surinder S. Saini, A. Wildeman and A. Kaushik. Both long and short germline D<sub>H</sub> genes exist in cattle. International Veterinary Immunology Symposium, Uppsala, Sweden, July 2001.
- **37.** Saini, S.S. and **Kaushik, A**. Structural and functional properties of bovine Vλ-light chains. **International Veterinary Immunology Symposium**, Uppsala, Sweden, July 2001.
- **38.** Cassady, R. L. and **Kaushik A.**, Increased negative B cell selection impairs neonatal IgM repertoire. **International Immunology Congress**, Stockholm, Sweden, July 2001.
- **39.** F. Shojaei, Surinder S. Saini, A. Wildeman and A. Kaushik. Both long and short germline D<sub>H</sub> genes exist in cattle. International Immunology Congress, Stockholm, Sweden, July 2001.
- **40.** Saini, S.S. and **Kaushik**, **A**. Structural and functional properties of bovine Vλ-light chains. **International Immunology Congress**, Stockholm, Sweden, July 2001.
- **41.** Cassady, R.L. and **Kaushik, A.** Increased negative B cell selection impairs neonatal IgM repertoire. "SLE: Targets for New Therapeutics" NIH Meeting, Washington DC, USA, January 2002.
- **42.** F. Shojaei, Surinder S. Saini and **A. Kaushik**. Unusually long germline DH genes contribute to the generation of exceptionally long CDR3H in bovine antibodies. American Association of Immunologists/FASEB Meeting, 2003. FASEB J. 17(7):C190.
- **43.** Saini, S.S. and **Kaushik, A.** Bovine IgG1 allotype. **International Veterinary Immunology Symposium,** Montreal, July 2004.
- 44. Koti, M., Kataeva, G. and Kaushik, A. K. Identification of novel bovine D<sub>H</sub> genes. International Immunology Congress. Rio de Janerio, Brazil, 2007 [Vet. Immunol. Immunopathol. 128 (2009) 318].
- **45.** Koti, M., Kataeva, G. and **Kaushik, A. K.** Organization of D-gene locus is distinct in cattle. **International Immunology Congress.** Rio de Janerio, Brazil, 2007.
- **46.** Koti, M., Nagy, E. and **Kaushik, A. K**. Construction of immunodiagnostic and therapeutic bovine antibodies as single chain Fv (scFv). International Veterinary immunology Symposium, Sao Paulo, Brazil, 2007 [Vet. Immunol. Immunopathol. 128(1):318-318.

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- Koti, M., Kataeva, G. and Kaushik, A. K. Significant germline D<sub>H</sub> gene size heterogeneity exists in cattle. International Symposium on Animal Genomics for Animal Health. Paris, France, October, 2007.
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- **49.** Koti, M., Kataeva, G. and **Kaushik, A. K**. Novel Conserved Genomic Sequence (CSGS) additions at VH-DH junction generate exceptionally long CDR3H in cattle antibodies. 21<sup>st</sup> Annual Meeting of the Canadian Society for Immunology. Mont-Tremblant, Quebec, April, 2008.
- **50.** Koti, M., Nagy, E. and **Kaushik, A. K**. Single point mutation in FR3 of engineered scFv affects viral neutralization without loss of epitope specificity. 21<sup>st</sup> Annual Meeting of the Canadian Society for Immunology. Mont-Tremblant, Quebec, April, 2008.
- 51. Koti, M., Kataeva, G. and Kaushik, A. K. 2008. Organization of DH-gene locus is distinct in cattle. Animal genomics for Animal Health Paris, France. (M. H. Pinard, C. Gay, P.P. Pastoret and B. Dodet; Dev. Biol. (Basel) 132:307-13)
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- **53.** Pasman, Yfke, Nagy, Eva and **Kaushik, Azad.** 2010. Monomeric and multimerized scFv neutralize bovine herpes virus-1. 23<sup>rd</sup> Canadian Society for Immunology Meeting, Niagra Falls, Ontario (April 23-26, 2010).
- 54. Pasman, Yfke, Saini, Surrinder, Smith, Elspeth and Kaushik, Azad. 2010. Organization of bovine lambda light chain genes on chromosome 17. 97<sup>th</sup> AAI Meeting, Baltimore, USA (May 8-11, 2010); J. Immunol., 184: 43.14. (Invited presentation at Block Symposium)
- 55. Pasman, Yfke, Nagy, Eva and Kaushik, Azad. 2010. Construction of multimerized scFv that neutralize Bovine Herpes Virus-1 97<sup>th</sup> AAI Meeting, Baltimore, USA (May 8-11, 2010); J. Immunol. 184: 52.12.
- 56. Pasman, Yfke, Nagy, Eva and Kaushik, Azad. 2010. Construction of multimerized scFv that neutralize Bovine Herpes Virus-1. 14<sup>th</sup> International Congress of Immunology, Kobe, Japan (August 22-27, 2010).
- 57. Pasman, Yfke, Saini, Surrinder, Smith, Elspeth and Kaushik, Azad. 2010. Organization of bovine lambda light chain genes. 14<sup>th</sup> International Congress of Immunology, Kobe, Japan (August 22-27, 2010).
- **58.** Pasman, Yfke, Saini, Surrinder, Smith, Elspeth and **Kaushik, Azad**. 2010. Restricted  $V_{\lambda}1-J_{\lambda}3-C_{\lambda}3$  recombinations encode the most  $\lambda$ -light chain repertoire in cattle. 9<sup>th</sup> International

Veterinary Immunology Symposium, Tokyo, Japan (August 16-20, 2010).

- 59. Pasman, Yfke, Nagy, Eva and Kaushik, Azad. 2010. Multimerized scFv neutralize Bovine Herpes Virus- 1 with higher efficacy. 9<sup>th</sup> International Veterinary Immunology Symposium, Tokyo, Japan (August 16-20, 2010) [Journal of Immunology. 2010.184: (1 Supplement) 52.12].
- **60.** Pasman, Yfke, and **Kaushik, Azad**. 2011. Functional scFvs against bovine herpesvirus-1 show differential cleavage and glycosylation patterns. 98<sup>th</sup> AAI Meeting, San Francisco, USA (May 13-17, 2011)
- **61.** Pasman, Yfke, and **Kaushik, Azad**. 2011. Differential cleavage and glycosylation patterns are noted in functional scFvs against bovine herpesvirus-1 expressed in *P. pastoris.* 24<sup>th</sup> Canadian Society for Immunology Meeting, Chateau lake Louise (April 8-11, 2011).
- **62.** Pasman, Yfke, and **Kaushik, Azad**. 2012. Partial organization of bovine variable-heavy chain gene locus and influence of recombination signal sequences (RSS) on variable region gene expression, Immunology 2012, American Association of Immunologists, May 2012, Boston, USA, J Immunol. 188: 42.6 (*Invited presentation at Block Symposium*)
- **63.** Pasman, Yfke, and **Kaushik, Azad**. 2012. Partial organization of bovine variable-heavy chain gene locus. Canadian Society for Immunology, June 15 -18, 2012, Annual meeting St. Johns Newfoundland.
- **64. Kaushik, A. K.** 2012. Functional aspects of single chain Fv and its multimers against Bovine Herpes Virus-1. Antibody Design and Discovery Conference, June 7-8, 2012, San Diego, USA (Distinguished Speaker).
- 65. Pasman Yfke, Nagy, Eva and Azad Kaushik. 2013. Recognition and neutralization of bovine herpesvirus-1 by bovine antibody variable heavy- and light-chain domains. American Association for Immunologists, Annual meeting Honolulu Hawaii U.S.A (May 2-7, 2013); J Immunol 2013 190:48.1.
- **66.** Pasman Yfke and **Azad Kaushik**. 2013. Elucidating the role of bovine heavy- and light-chain variable domains in polyspecific antigen-binding. American Association for Immunologists, Annual meeting Honolulu Hawaii U.S.A (May 2-7, 2013); J Immunol 2013 190:141.15.
- 67. Yfke Pasman and Azad K. Kaushik. 2013. Antigenization of bovine immunoglobulin variable regions for development of novel vaccines. 15<sup>th</sup> International Congress of Immunology Milan Italy (August 22-27,

2013);<u>http://www.frontiersin.org/MyFrontiers/Events/AbstractDetails.aspx?ABS\_DOI=10.</u> 3389/conf.fimmu.2013.02.01176 (Invited presentation).

68. Yfke Pasman and Azad K. Kaushik. 2013. Polyspecific antigen binding by bovine immunoglobulin heavy- and light-chain variable domains. 15<sup>th</sup> International Congress of Immunology Milan Italy (August 22-27, 2013);<u>http://www.frontiersin.org/MyFrontiers/Events/AbstractDetails.aspx?ABS\_DOI=10.</u> 3389 /conf.fimmu.2013.02.01177

- 69. Yfke Pasman and Azad K. Kaushik. 2013. Polyspecific antigen binding by individual bovine immunoglobulin heavy- and light chain variable domains. 10<sup>th</sup> International Veterinary Immunology Symposium, Milan Italy. (August 28 September 1, 2013).
- 70. Yfke Pasman and Azad K. Kaushik. 2013. Bovine Herpesvirus-1 epitope grafting onto bovine immunoglobulin CDR3H to induce protective immunity. 10<sup>th</sup> International Veterinary Immunology Symposium, Milan Italy. (August 28 September 1, 2013).
- 71. Azad K. Kaushik. 2014. Engineering bovine antibodies to develop novel therapeutics and vaccines. 6<sup>th</sup> Annual International Congress of Antibodies 2014. Dalian, China. (April 25 28, 2014).
- 72. Pasman Yfke and Azad Kaushik. 2014. Differential contribution of variable heavy and variable light chain domains in viral epitope recognition and neutralization function. Immunology 2014. American Association for Immunologists, Annual meeting Pittsburgh, U.S.A (May 2-6, 2014); J Immunol 2014 192:140.11.
- **73.** Pasman Yfke, Daniele Merico and **Azad Kaushik**. 2015. Differentially expressed immune related genes in bovine neonatal development. American Association for Immunologists, Annual meeting New Orleans, U.S.A (May 2-6, 2014); J Immunol 2015 194:146.2.
- 74. Pasman Yfke, Daniel Merico and Azad Kaushik. 2015. Differentially expressed immune related genes in bovine neonatal development. American Association for Immunologists, Annual meeting New Orleans, U.S.A (May 2-6, 2015); J Immunol 2014 194:146.2 (Invited Block presentation).
- 75. Azad Kaushik and Pasman Yfke. 2016. Functional differences exist in contribution of V<sub>H</sub> and V<sub>L</sub> from polyspecific IgM and monospecific IgG antibodies in antigen recognition and virus neutralization functions. American Association for Immunologists, Annual meeting, Seattle, USA (May 13-17, 2016) [J Immunol 2016 196:216.2].
- 76. Azad Kaushik, Pasman Yfke and Daniele Merico. 2016. IGHV and IGHD encoding antibodies with exceptionally long CDR3H are predominant in the bovine neonatal B cells. American Association for Immunologists, Annual meeting, Seattle, USA (May 13-17, 2016). [Journal of Immunology 2016. 196: (1 Supplement) 77.2].
- 77. Pasman Yfke and Azad Kaushik. 2016. V<sub>H</sub> and V<sub>L</sub> from polyspecific IgM and monospecific IgG antibodies contribute differentially to antigen recognition and virus neutralization function. 16<sup>th</sup> International Congress of Immunology (August 21-26, 2016), Melbourne. Australia (Eur. J. Immunol. 2016. 46(Suppl.1): 801).
- **78.** Pasman Yfke and **Azad Kaushik.** 2016. Exceptionally long CDR3H of bovine scFv antigenized with BoHV-1 B-epitope generates specific immune response against the

targeted epitope. 16<sup>th</sup> International Congress of Immunology (August 21-26, 2016), Melbourne. Australia (Eur. J. Immunol. 2016. 46(Suppl.1): 1100).

- **79.** Pasman Yfke, Daniele Merico and **Azad Kaushik.** 2016. *IGHV* and *IGHD* encoding antibodies with exceptionally long CDR3H are most expressed at birth in the bovine neonate. 16<sup>th</sup> International Congress of Immunology (August 21-26, 2016), Melbourne. Australia (Eur. J. Immunol. 2016. 46(Suppl.1): 871).
- 80. Yfke Pasman, Daniele Merico and Azad K. Kaushik. 2016. Exceptionally long CDR3H of bovine scFv provides a suitable scaffold for antigenization with conformational B-epitope capable of inducing specific immune response. 11<sup>th</sup> International Veterinary Immunology Symposium (August 16-19, 2016), Gold Coast, Australia.
- **81.** Yfke Pasman and **Azad K. Kaushik**. 2016. Development of bovine humoral neonatal immunity is characterized by predominant expression of *IGHV* and *IGHD* encoding antibodies with exceptionally long CDR3H. 11<sup>th</sup> International Veterinary Immunology Symposium, Milan Italy (August 16-19, 2016). Gold Coast, Australia.
- 82. Kaushik, A. K. 2016. 'Exceptionally long CDR3H of bovine scFv antigenized with BoHV-1 B-epitope generates specific immune response against the targeted epitope (Session speaker), 2<sup>nd</sup> International Conference on Antibodies and Therapeutics (July 11-12, 2016), Philadelphia, USA.
- **83.** Damani-Yakota, P., A. Kaushik, J.C. Tefler and C.L. Baldwin. 2016. Variegated gene expression of WC1, a hybrid PRR/Co-receptor on single-cell memory  $\gamma\delta$  T cell clones. U.K.

#### **Distinguished Invited Lectures**

- **84.** Peritoneal B cell and autoimmunity' Round Table Conference on Autoimmunity, Pasteur Institute, Paris, June 1987.
- **85.** Vh11: a new murine gene family. University of Texas Medical Branch, Galveston, Texas 77550, April 1988.
- **86.** Idiotype and structure of autoantibodies reactive with bromelain treated red blood cells. Mount Sinai School of Medicine, New York, May, 1988.
- **87.** 'Molecular analysis of natural autoantibodies'. National Institute of Immunology, New Delhi, September 1988.
- 88. Phenomenon of autoimmunity, University of Missouri, Columbia, February 1990.
- **89.** Construction of immunoglobulin repertoire, University of Geneva Medical School, Geneva, September 1990.
- 90. Idiotype: Concepts and Applications. University of Guelph, Guelph, 1991.
- **91.** Construction of antibody repertoire. University of Guelph, Guelph, 1992.

- **92.** B lymphocyte, Immunodeficiency and Autoimmunity, Mount Sinai School of Medicine, New York, December 1994.
- **93.** Molecular immunobiology of self reactive autoantibodies, Molecular biology 1995 Conference, San Diego, 1995.
- **94.** CDR3H length in health and disease, Oklahoma Medical Research Foundation, Oklahoma City, 1997.
- **95.** Current perspectives on B-1 lymphocytes and immune response, International Centre of Genetic Engineering and Biotechnology, New Delhi, 1998.
- **96.** 'Novel insight through bovine immunoglobulin genes', Department of Molecular Biology, University of Guelph, 1999.
- **97.** Of mice, cattle and antibodies, Ohio State University Children's Hospital, February 2001.
- **98.** Novel insight into antibody diversification from cattle. International Veterinary Immunology, Symposium, Uppsala, Sweden, July 2001.
- **99.** Bovine Antibody gene Technology in Health and Disease, Angenics, University of Guelph, Guelph, November, 2001.
- **100.**Bovine Antibody Transgenesis, Albert Einstein College of Medicine, New York, USA, 2004.
- **101.** The dogma of cattle antibody', Institute for Molecular Biology and Biotechnology, Vrije Universiteit Burssel, Burssel, Belgium, October, 2005.
- **102.** Immunoglobulin genetics, Round Table Meeting, INSERM Unit, L'Eclole the Medicine, Paris, France, February, 2006.
- **103.** Antibodies: Structure, Function and Application. South Dakota State University, Brookings, USA, November 2, 2007.
- **104.**Translational aspects of bovine antibodies in animal health. Ontario Ministry of Agriculture and Food, Guelph, Ontario, Canada, November 28, 2007.
- **105.**Bovine antibody genetics in health and disease, IMGT, CNRS, Universite Montpellier 2, Montpellier, France, February 2010.
- **106.** Functional aspects of single chain Fv and its multimers against Bovine Herpes Virus-1, Antibody Design and Discovery Conference, June 7-8, 2012, San Diego, USA (Distinguished Speaker).
- **107.** Novel structural and functional aspects of bovine antibody suitable for engineering new anti-viral drugs and vaccines. Faculty of Veterinary Medicine, Lala Lajpat Rai University of veterinary and Animal Science, Hisar, India, May, 2014.
- **108.**Cow Megabodies for Better Human Health, National Academy of Agricultural Sciences, New Delhi, India, January, 2015.
- **109.** Exceptionally long CDR3H of bovine scFv antigenized with BoHV-1 B-epitope generates specific immune response against the targeted epitope (Session speaker), 2<sup>nd</sup>

International Conference on Antibodies and Therapeutics (July 11-12, 2016), Philadelphia, USA.

#### **Publications Summary**

Book	Journal Article	Book Chapter	Book Reviews/ Editorial/Other	Conference Presentations	Distinguished Speaker
2	68	9	11	84	26
Total:		88		110	

#### **Research Citations in Text books**

- Clinical Immunology of the Dog and Cat, 1<sup>st</sup> ed. (1999) Michael J. Day, ISU Press, Iowa, Chapter 15, p. 284.
- The Genetics of Cattle, 1<sup>st</sup> ed. (1999) Ruedi Fries and Anatoly Ruvinsky, CABI (www.cabi.org), Chapter 7
- Veterinary Immunology: An Introduction, 7<sup>th</sup> ed. (2004) I. Tizard, W.B. Saunders Co., Chapter 14, p.164.

#### **DNA Sequences Deposited and Annotated**

- Bovine Immunoglobulin Genes (V<sub>H</sub>- D<sub>H</sub>- J<sub>H</sub>- Cμ/Cγ; Vλ-Jλ-Cλ) 121
- Bovine D-genes and RSS (Dh1, Dh2 and DH3/RSS) 8
- Murine Immunoglobulin Genes (V<sub>H</sub>- D<sub>H</sub>- J<sub>H</sub>; Vκ-Jκ) -110
- Bovine D-gene locus (~35kB; yet to be annotated)
- ScFv DNA Sequences (yet to be annotated)
- Bovine Neonatal and Maternal Transcriptiome (yet to be annotated)

#### **Graduate Thesis Supervised**

I have trained 5 postdoctoral fellows (PDF), 3 PhD students and 5 theses based MSc students as part of my research program. I currently supervise 1 PDF and another graduate student is being recruited from fall, 2016. Two of the graduated students from my laboratory are faculty members at Canadian universities (Madhuri Koti, School of Medicine, Queen's University, Kingston; Byram Bridle, Ontario Veterinary College, University of Guelph, Guelph; Robin Cassady, The Roslin Institute, Edinbrough, UK) while one is a National Manager at the Canadian Food Inspection Agency (Dr. Surinder S. Saini). Others are in senior positions in the industry (Joy Knott, Becton and Dickinson, San Diego, USA; Farbod Shojaei, Pfizer/Bionomics Ltd, San Diego, USA). My research endeavors extend to undergraduate teaching as I have trained over 25 undergraduate students and 5 of them have contributed to 6 peer-reviewed research publications in high impact journals.

#### PhD

- Surinder Saini, <u>PhD Thesis</u> (1999). "Molecular immunogenetics of bovine antibody", University of Guelph, Guelph, Ontario, Canada.
- Madhuri Koti, <u>PhD Thesis</u> (2007). "Immunogenetics of bovine antibody diversity and construction of recombinant therapeutic antibody". University of Guelph, Guelph, Ontario, Canada.
- Yfke Pasman, <u>PhD Thesis</u> (2015). "Bovine antibody genetics, structure and antigenization for disease prevention". University of Guelph, Guelph, Ontario, Canada.

#### MSc

- Joy Knott, <u>MSc Thesis</u> (1995). "Construction of primary antibody repertoire in kappadeficient mice". University of Guelph, Guelph, Ontario, Canada.
- Byrum Bridle, <u>MSc Thesis</u> (1997). "Age and strain related influences on commercially raised chicken peripheral blood lymphocytes". University of Guelph, Guelph, Ontario, Canada.
- Robin Cassady, <u>MSc Thesis</u> (2000). "Increased negative selection during ontogeny impairs IgM antibody repertoire", University of Guelph, Guelph, Ontario, Canada.
- F. Shojei, <u>MSc Thesis</u> (2001). "Molecular aspects of bovine D-genes". University of Guelph, Guelph, Ontario, Canada.
- Yfke Pasman, <u>MSc Thesis</u> (2010). "Structural and functional aspects of engineered antibody against Bovine Herpes Virus-1. University of Guelph, Guelph, Ontario, Canada.

#### Post-doctoral Training

1. Dr. Alpana Nangpal (Murine VLambda genes)	1993-1995
2. Dr. Arvind Kashyap (Murine VH Genes)	1995-1996
3. Dr. Surinder Saini (Bovine antibody transgenesis)	2000-2003
4. Dr. Raspal Bhogal (Bovine immunoinformatics)	2009-2010
5. Dr. Ashish Sachan (Therapeutic antibodies)	2013-2016

#### **Thesis Examination**

University of Guelph:	
1. Y. F. Tian, MSc, 1991 (Microbiology)	9. Byram Bridle, MSc, 1997 (Pathobiology)
2. A. DeLaPana, MSc, 1994 (VMI)	10. S. S. Saini, PhD, 1999 (Pathobiology)
3. J. Knott, MSc, 1995 (VMI)	11. M. Mohammad, PhD, 1999 (Ani.Poultry Sc.)
4. G. Appleyard, PhD 1995 (VMI)	12. F. Shojaei, MSc, 2001 (Pathobiology)
5. E. Gallo-Hendrikx, PhD, 1996 (Molec. Biol.)	13. Jillian E. A. Tarling, 2014, PhD (Env. Biol.)
6. Nancy Tout, PhD, 1997 (Microbiology)	14. Yfke Pasman, 2015, PhD (Molec. & Cell Biol.)
7. H. S. Banga, PhD, 1997 (Pathobiology)	15. Sherise Charles, 2016, MSc (Molecular and Cellular Biology; Chair)

8. N. Reinhardt, DVSc, 1997 (Clinical studies)

#### National and International:

14. Ziyuan Zhang, PhD, 2002 (Immunology), University of Manitoba, Winnipeg, Manitoba

15. Aarti, PhD, 2010 (Immunology), Indraprastha University, New Delhi, India

16. Jenni Liljavirta, PhD, 2014 (Immunology), University of Helsinki, Finland

#### **PhD Qualifying Examination**

- 1. John Papp, 1992 (Vet. Microbiology and Immunology)
- 2. Greg Appleyard, 1993 (Vet. Microbiology and Immunology)
- 3. Weerapong Koykul, 1993 (Biomedical Science)
- 4. Surinder S. Saini, 1996 (Vet. Microbiology and Immunology)
- 5. Ted Fjallman, 2004 (Environmental Biology)
- 6. Nina Weisser, 2005 (Environmental Biology)
- 7. X. Xie, 2006 (Environmental Biology)
- 8. Amanda Stefanson, 2015 (Human Health and Nutritional Sciences)

#### **Student Advisory Committee**

1. Malcolm Weir, MSc, 1993.	8. Nancy Reinhardt, DVSc, 1997
2. Phillip Ng, MSc, 1994.	9. L. Braz-ruivo, DVSc, 1997
3. Greg Appleyard, PhD, 1995.	10. J. Reddy, PhD, 1997
4. Shirley, Furesz, PhD, 1996.	11. B. Messingher, DVSc, 1998

- 5. S. Reddy, PhD, 1996
- 6. Weerapong Koykul, PhD, 1996
- 7. Nancy Tout, PhD, 1997

15. Xuemei Xie, Ph D, 2005-2009

Mollie Ferassis, DVSc, 1999
 13. Nina Weisser, MSc, 2003-05
 14. Nina Weisser, PhD, 2005-08

#### **Undergraduate Student Research Training**

Department/Program	Student	Semester, Year
Biomedical Science	Bev Walter	F, W, S, 1993-1994
	Melissa Gray	S, 1994
	Mark R. Jonkman	W, S, 1994
	Elizabeth Davidson	F, 1994; W, 1995
	Wai-May Lim	F, 1994; S <i>,</i> 1995
	Mark Belletrutti	F, W, 1995-1996
	Jana Cartier	W, 1999
	F. Zelster	S, 1999
	Bethany Lowe	W, 2000
	Melissa Cogswell	W, 2001
	Pravin Vijayan	W, 2004
	Timothy Patterson	W, 2005
	Kathryn Smith	W, 2009
	Miyuki Kumagai	F, 2010, F2011
Molecular Biology and Genetics	Jennifer Richardson	F <i>,</i> 1994
	Andrea Kurtz	F and W, 2002
	Christina Southey	F and W, 2003-04
	Brooke Janson	S, 2007
	Daniel Grosberg	F, 2013
	Harish Kandavel	W2017, F, 2017
Veterinary Medicine	S. Ng	S, 2000
Microbiology	Andrea E. Jacob	F, 1997
	Adam Crossley	S, 2003
	Heidi Machina	F, 2003
	Fred Zelster	F <i>,</i> 2004
	Lindsay Baltjes	W, 2005
Arts and Science	Richard W. Gilbert	F, 2009

#### **Teaching Expertise**

Veterinary Immunology, Veterinary Clinical Immunology, General Immunology, Immunopathology, Immunity to Infection, Autoimmunity, Immunogenetics, Veterinary Infectious Diseases, suitable at professional DVM, graduate and undergraduate level.

#### **Teaching Philosophy**

My teaching philosophy, based on the principle of liberal education, continues to aim at encouraging active and stimulated personalized learning by students via interactive illustrated lectures and discussions. Various approaches include:

- Use of multi-media, online live lecture podcasts to help enhance individualized and independent integrated learning in proper context.
- Extensive clinical or practical situations are cited to emphasize the relevance of basic knowledge of the immune system as applied to health and disease, a style especially suitable for learning immunology.
- Specific emphasis on 'structured reflection, concepts and principles to enhance learning experiences.
- Creating opportunities for students to engage actively in the classroom, e.g., iClickers or discussion questions.
- Encourage active learning by making them understand that they learn by themselves per se within the context of lectures and brief guided notes.
- Facilitate learning where a student is an active processor of information and creator of personal knowledge.
- Engaging students via co-operative learning approach

#### **Teaching Profile**

My teaching experience has been broad and spread across various undergraduate and graduate courses, such as, Veterinary Immunology, Elective in Clinical Veterinary Immunology, Health Management (4th year DVM clinical rotations), Introductory Immunology (3rd year level BSc), Immunology II (4th year BSc), First Year Seminar (Immunity and Health) and Advances in Immunology and Immunochemical Techniques (graduate level). I contributed to other DVM courses in Pathology and Internal Medicine and also at graduate level (Immunobiology). My teaching approach encourages the principle of quality liberal education aimed at encouraging active and stimulated personalized learning by students via interactive illustrated lectures and discussions. I use multi-media and clinical or practical situations to enhance understanding of the immune system, a style especially suitable for learning complex concepts of the immune system. I like to emphasize on structured reflection, concepts and principles as basic elements of learning. First, I designed an elective in veterinary clinical immunology for 4th year DVM students, which required senior DVM students to immerse in Clinical Veterinary Immunology. I developed new clinical cases, using materials received in the clinical immunology laboratory for investigation, for teaching DVM students during 4th year clinical rotations. I taught veterinary immunology to DVM students from 1992 to 2002 that led me to develop new learning materials emphasizing the principle of Evidence based Veterinary Medicine. I contributed significantly to the pedagogy of veterinary immunology in the development of new curriculum of the DVM phase I that took professional competencies into consideration. I designed the new curriculum for teaching of veterinary immunology in the phase I, which I implemented successfully from 2000 to 2002. I have significantly contributed to the pedagogy of 3rd year level Introductory Immunology and 4th year level Immunology II (undergraduate) and Advances in Immunology and Immunology Techniques (graduate level) courses.

Five undergraduate research project students contributed to six peer-reviewed research publications in the mainstream immunology journals. My mentoring of graduate students has been a rare joy who have excelled, as evidenced by the external examiner's assessment and their placement as faculty or senior positions in the industry and government. Overall, I have trained ~1000 Veterinarians, thousands of undergraduate students and hundreds of graduate students in the discipline of immunology. My commitments to higher learning have contributed to literature that is cited in the textbooks.

#### **Learning Materials**

- Veterinary Immunology Laboratory Manual and clinical Case Studies
- Basic Techniques in Immunology Manual

#### **Courses Taught**

#### Graduate:

Immunobiology, 91-610, (1991-1996, 2009-13) Topics in Immunology, 91-611, (1991, 1992\*, 1993) Special Topic in VMI\*, 91-695, (1992) Guest lectures: General Pathology (1997-98); Vet. Internal Medicine (1999-2002) Advances in Immunol. & Immunochem. Techniques, MICR 6423, (2003-04; 2005-08\*)

#### Undergraduate:

Immunology and Serology/ Immunology I, MICR3230;65-409/410, (1992-1995, 1999-2016\*) Veterinary Immunology, 93-355, (1994, 1995\*, 1996\*, 1997-1999, 2000-02\*) Health management, 4th year rotation, 93-485, (1992-1995) Biomedical research Project, 98-450/4511/4521, (1992-1997, 1999-2005) Elective in Clinical Immunology\* (1992, 1993-1997) Immunology II, MICR4240\*; MICR4310\*/MICR4230, (1994-2002; 2003\*, 2005-17\*); Immunology II, MICR4530, (W2012-16\*) Topics in Microbiology, MI4310/4320; Research Project I/II, MICR4240, (2002-03, 2008) \* Immunity and Health, Univ1200: (2006-09)\*

[\*Course Co-ordinator]

#### **Administrative and Community Service Profile**

I have contributed to a wide spectrum of administrative and service functions at the university and at national and international levels. I supervised and provided clinical immunology service for a decade (1992-2002), examining 450-500 clinical specimen/year. It made a significant impact in Ontario and Canada for the quality of diagnostic service and introduction of new tests not available elsewhere. Several DVSc degree program students utilized clinical immunology service for their thesis research leading to collaborative publications. Several clinical reports involving immunodeficiency or immune mediated disease were published in professional veterinary journals, including a review of a clinical immunology textbook. I was invited to be on the editorial board of the Journal of Veterinary Allergy and Clinical Immunology. The impact of the clinical immunology diagnostic service was evidenced by a positive feedback about the quality of service from the Veterinarians and farmers across Ontario and in Canada. The introduction of new tests led to leadership in North America with equine test samples tested from as far as Texas, USA.

As Chair of Ontario Graduate Studies Scholarship Award Committee Panel, I evaluated and deliberated with the panel members to develop consensus to rank the candidates on merit for award of a scholarship.

I provide extensive peer review support to various high impact journals (for example, Journal of immunology, Science) and national and international granting agencies (for example NSERC Canada, NIH, CIHR). I am on the editorial board of several journals related to the immunology field where I provide editorial advice and support. I volunteer on a national panel of scientists for 'Ask a scientist' and act as an educational resource for immunology-related questions. I have chaired several symposia or scientific sessions at national (Canadian Society for Immunology) and international scientific meetings (American Association of Immunologists, International Veterinary Immunology Symposium, International immunology Congress).

Given my international leadership in the field of antibody genetics, I have been nominated and elected to honorary positions as IMGT Expert for bovine antibody genes (France), Curator of bovine immunoglobulin genes by Comparative Immunoglobulin Workshop (University of Iowa, USA) and Consultant US Veterinary immune Reagent Network (Massachusetts, USA) where I offer my professional advice and contribute towards proper immunoglobulin nomenclature. These are honorary invited positions in recognition of my scientific contributions and leadership. In 2015, I was nominated and elected as the member of the important American Association of Immunologists (AAI) Veterinary immunology Committee for a period of three years.

In support of non-professional community outreach, I took the leadership role as the President of the National Alliance of Indo-Canadians and Chair of the Organizing Committee, upon being elected by various Indo-Canadian community organizations, to host a community reception for the visiting Indian Prime Minister Narendra Modi in Toronto (April 16, 2015). The international level event was presided and led by the Prime Minister Stephen Harper. This was a major public event in honor of the visiting Prime Minister with an international impact that helped enhance Canada-India bilateral relationship to a new level.

#### Professional

- Co-Chair, Session on "*The Immune Repertoire*", American Association of Immunologists Meeting/Experimental Biology, 1998, San Francisco, April 18-22, 1998.
- Chair, Session on "*Ig and TcR Genes*", 5<sup>th</sup> International Veterinary Immunology Symposium, Ludhiana, India, November 1998.
- Co-Chair, *'Lymphocyte Development'* Workshop, Canadian Society for Immunology Meeting, Chateau Lake Louise, April, 2001.
- Co-Chair, Session on "*Comparative Immunoglobulin Structure and Function*", American Association of Immunologists Meeting/Experimental Biology, 2008, San Diego, April 5-9, 2008.
- Chair, Ontario Graduate Studies Scholarship Award Committee Panel (2002), Canada.
- Member, NIH Grant Review Panel on 'Specialized Centres of Research on Systemic Lupus Erythematosus' (2002), USA.
- Member, American Association of Immunologists, Canadian Society of Immunology, Canadian Society of Microbiology, New York Academy of Science, Academy of Veterinary Allergy & Clinical Immunology.
- Ad hoc Reviewer, Journal of Immunology, Autoimmunity, Viral Immunology, Molecular Immunology, Developmental and Comparative Immunology, Veterinary Immunology and Immunopathology, Veterinary Microbiology, Canadian journal of Microbiology, Journal of Molecular Recognition, Plos One etc.
- Ad hoc Reviewer, Grant-in-Aid, Canadian Arthritis Society Grant-in-Aid, Medical Research Council, NSERC Canada, NIH SCOR Program, Health Canada, Michael Smith Foundation for Health Research, Canadian Foundation for Innovation

- Editor-at-Large, Marcel Dekker Inc., New York
- Member, Editorial Board: Journal of Veterinary Allergy & Clinical Immunology, Journal of Vaccines and Immunization, Noble Research Publishers Limited (<u>http://www.nobleresearch.org/Journals/JVI/Editorialboard.aspx</u>); Journal of Biomedical Sciences; and Research in Immunology
- Member, College Library Committee (1992-96; 2015-16)
- Member, Department Graduate Studies and Research Committee (1996-99; 2016-)
- Member, Pet Trust Research Award Panel (1999-2002)
- Member, Ontario Graduate Studies Scholarship Award Committee (2001)
- Member, Department T&P Committee (2003)
- Chair, Department Biosafety Committee (2003-04)
- Chair, Ontario Graduate Studies Scholarship Award Committee Panel (2002)
- Member, NIH Review Panel on SCOR on SLE (2002)
- Member, Peer Review Panel, Innovative Science Competition, Health Canada (2003)
- Chief, Clinical Immunology Service, 1992-2002
- Member, University of Guelph Faculty Association Council (2004 -07)
- Member, University Student Service Fee Committee (2005 -06)
- Member, UGFA Health and safety Committee (2005 -06)
- Member, University Student Judicial Committee (2006-09)
- Reviewer, BC Innovation Council: BCIC Innovation Scholars (2010)
- Chair, Vaccines-2 Mini Symposia at the 16<sup>th</sup> International Congress of Immunology, Melbourne, Australia (2016)

#### **Current Affiliations/Memberships**

- American Association of Immunologists
- Canadian Society for Immunology

#### Media Coverage (Professional Activities)

- 1. http://news.uoguelph.ca/2012/07/cow-antibodies-offer-hope-for-human-diseases/
- 2. http://www.internationalinnovation.com/build/wp-content/uploads/2014/11/p94-
- 95\_Azad\_Kumar\_Kaushik\_Intl\_Innovation\_161\_Research\_Media.pdf

3. Youtube: <u>https://youtu.be/m6VBJJF2BjU</u> (CTV Kitchener news)

- 4. <u>http://cou.on.ca/articles/cow-antibodies-may-hold-cure-fighting-human-diseases-u-g-study/</u>
- 5. https://www.guelphtoday.com/local-news/cow-antibody-could-help-fight-cancer-443695

6. http://www.agcanada.com/2016/11/cow-antibodies-show-a-path-to-fighting-human-disease

7. <u>http://news.uoguelph.ca/2016/10/cow-antibodies-may-hold-cure-fighting-human-diseases-study/</u>

8. <u>http://www.manitobacooperator.ca/news-opinion/news/cow-antibodies-show-a-path-to-fighting-human-disease/</u>

9. <u>http://yourontarioresearch.ca/news/2016/10/guelph-today-cow-antibody-help-fight-cancer/</u>10. <u>http://www.guelphnow.ca/npps/story.cfm?nppage=2358</u>

11. http://exchangemagazine.com/morningpost/2016/week43/Tuesday/16102535.htm

#### **Community Support**

- Founder President, World Brahman Federation Canada that promotes Dharma and values in the society (www.wbfcanada.net)
- Founder Secretary General, Global Brahman Federation (www.gbcnet.org)
- Founder President, Guelph Hindu Heritage Cultural Society, Guelph (Influenced the City Government to change fire by-laws so that Hindus, Sikhs, Jains and others could normally celebrate Deepawali festivities at home with Canadian friends of other faith to promote celebration of cultural diversity
- Value based education to youth to become law-abiding citizens who are an asset to the society and contribute towards advancing aspirations as Canadians.
- Motivational Speaker and Influencer in the community on matters concerning human consciousness, Dharma and civilization.
- Chair, Organizing Committee for community reception for Indian Prime Minister Mr. Narendra Modi, presided by Prime Minister Stephen Harper in Toronto (2015) that helped enhance Canada-India relationship
- President, Overseas Friends of BJP Canada, Toronto, that aims to create bonds among Canadians, people of Indian origin and Indians.
- President, National Alliance of Indo-Canadians
- Chair, Indo-Canadian Harmony Forum

#### **Personal Interests**

- Reading and Writing
- Climbing [Organized two expeditions to Himalayas and climbed two peaks: Mount Ladhaki (18,600' ft) and Mount Thailoo (20,000' ft)]
- Travelling
- Arts and Music